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DD

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/942,067	10/01/97	BENSUN S	4356

HM22/0217

PE APPLIED BIOSYSTEMS
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EXAMINER	
HOUTTEMAN, S	

ART UNIT	PAPER NUMBER
1634	8

DATE MAILED: 02/17/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/942,067	Applicant(s) Benson et al.
	Examiner Scott Houtteman	Group Art Unit 1634

☐ Responsive to communication(s) filed on _____ .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-37* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-37* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Applicant's response, filed 122/98, has been carefully considered with the following effect:

The rejections of paragraphs 2, Office action mailed 10/1/98, has been maintained.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The amendment filed 12/2/98 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Formula on page 20 have been materially altered. The attachment point of the "-O-B_1" side group has been changed from a nitrogen atom to the adjacent phosphorous atom. No support for this modification was pointed out nor was it found.

Applicant is required to cancel the new matter in the reply to this Office action or point out the support for this amendment.

4. Claims 1-37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lee et al., Nucleic Acids Res. 20(10):24712-83 (1992) for reasons of record.

5. Applicant argues that Lee does not teach the R_1 and R_7 substituents and cannot render claim 1 obvious. This argument is not persuasive. Lee teaches several of the claimed R_1 and R_7

embodiments, for example chlorine and lower alkoxy (See Lee page 2478, Fig. 5; b, c, d. The claims are not limited to the R_1 and R_7 taken together.

6. Applicant argues that Lee does not teach phosphoramidate or phosphoramidite. This argument is not persuasive. Claims 1-27 and 35-37 are not so limited. With respect to claims 28-34 the claims are not limited to any specific phosphoramidate compound but merely recite a phosphoramidate compound made up of the claim 1 dye. Accordingly, Lee need only suggest a similar generic concept.

Lee provides this in the recitation of "Dye primers." It is well known and a matter of common knowledge that a nucleic acid sequencing method requires a label attached to the nucleic acid. There are two general methods of attaching the label (1) a labeled primer and (2) a label incorporated during the extension reaction. The main focus of Lee is the latter. Lee, however, also suggests labeling the primer also. It is this suggestion that provides support for the phosphoramidate intermediates, these are the reagents used in the synthesis of the labeled primer.

Furthermore, the specification evidences that the use of labeled phosphoramidate reagents to label primers is known in the art. See for example, the specification, page 25. Accordingly, given the Lee suggestion to attach the label the primer, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to attach the Lee label using the labeled phosphoramidate reagents.

7. Applicant asserts "the relationship between molecular structure and spectral properties in fluorescent dyes is complex and unpredictable." This argument is not persuasive. Attorney assertions, unsubstantiated by an evidentiary showing, for example, a factual showing under Rule 132, are given no weight. Furthermore an analysis of Lee shows that Lee was able to synthesize four separate labels each with a distinct spectral property so that the four labels can be detected in a single reaction vessel. The successful production of four dyes with compatible fluorescent spectra is evidence that these spectral are not altogether unpredictable. It most likely depends upon what is known about particular dyes ring structures and particular side groups. The effects of some combinations may be unpredictable but most likely the effects of other are entirely predictable, for example, those combinations that are closely chemically related to previous well understood combinations from the relevant literature.

8. Applicant argues that "improvements translate to larger peaks and improved DNA sequencing and fragment analysis results and that these results are unexpected. This argument is not persuasive for several reasons. (1) There is no comparison with the prior art to illustrate the "improvements." (2) The scope of the alleged improvements in not commensurate with the scope of the claimed subject matter. The claims recite a wide variety of side groups: various halides, phenyl, "substituted" phenyl, "substituted polycyclic aromatic" etc. The specification contains no evidence that a reasonable number of the vast genera such as "substituted polycyclic aromatic" side groups will result in the "improvements."

9. Finally, applicant argues that Lee is non-enabling in comparison the present specification. This argument is not persuasive. While at first blush it appears that the Lee teaching is meager with respect to applicants disclosure. This, however, is appropriate under the circumstances.

The standard for enablement of a reference in providing a *prima facie* showing of obviousness, is lower than that of the specification. There is a statutory enablement requirement; under 35 U.S.C. § 112, first paragraph; imposed on an inventor's specification. The specification must enable the art skilled to practice the invention without undue experimentation. This higher standard is part of the basic *quid pro quo* public policy insuring that the inventor provide to the public a full disclosure of the invention in return for the grant of monopoly from the government. In sharp contrast, there is no such requirement on a reference to provide evidence of obviousness under 35 U.S.C. § 103.

Furthermore, Lee need not render obvious the full scope of the claims but merely a single embodiment within these claims. As stated previously, Lee suggests the claimed labels having side groups such as the lower alkoxy when R_7 is taken separately from R_1.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the mailing date of this final action.

11. Papers relating to this application may be submitted to Technology Center 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Technology Center 1600 Fax numbers are (703) 305-3014 and 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 308-3885. The examiner can normally be reached on Tuesday-Friday from 8:30 AM - 5:00 PM. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center receptionist whose telephone number is (703) 308-0196.

Scott Houtteman
February 16, 1999

Scott W. Houtte

SCOTT W. HOUTTEMAN
PRIMARY EXAMINER